

IN THE SPECIFICATION

Replace the originally filed specification with the new substitute specification of **APPENDIX A**.

IN THE CLAIMS

Amend claims 2-6, 10, 11, 13, 14 and 16 to read as follows:¹

2. (Twice Amended) The method according to claim 10, wherein the inhibition of the poly(ADP ribose) polymerase is caused by the expression of a dominant negative transgenic poly(ADP ribose) polymerase.

3. (Amended) The method according to claim 2 or 10, wherein the inhibition of the poly(ADP ribose) polymerase has been effected by a transgenic operation.

4. (Twice Amended) The method according to any one of claims 2, 3 and 10, wherein the mammal used is a transgenic mouse.

5. (Twice Amended) The method according to any one of the claims 2, 3, 4 and 10, wherein the potentially carcinogenic agents are administered by topical application.

6. (Twice Amended) The process according to any one of claims 2, 3, 4, 5 and 10, wherein the mammal expresses transgenically the DNA construct shown in Figure 1.

10. (Amended) A method for identifying carcinogenic agents, said method comprising (i) administering one or more potentially carcinogenic agents to a transgenic mammal having a

¹ Consistent with the requirements of 37 CFR §1.121, a marked-up copy of the amended claims 2-6, 10, 11, 13, 14 and 16 is set forth in **APPENDIX E** herein and a clean copy of all pending claims in the application is set forth in **APPENDIX F** herein.

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transgenically modified genome comprising a DNA repair disturbance caused by a transgene of the transgenic mammal inhibiting poly (ADP ribose) polymerase, and (ii) comparing said transgenic mammal administered one or more potential carcinogenic agents, with a transgenic mammal not administered said one or more potential carcinogenic agents, wherein development of tumor in the transgenic mammal administered said one or more potential carcinogenic agents, indicates that a potential carcinogenic agent is a carcinogenic agent.

11. (Amended) A transgenic mammal comprising a genome comprising a DNA repair disturbance caused by a transgene of the transgenic mammal inhibiting poly(ADP ribose) polymerase.

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13. (Amended) The transgenic mammal of claim 11, wherein the inhibition of the poly(ADP ribose) polymerase is caused by expression of a dominant negative transgenic poly(ADP ribose) polymerase.

14. (Amended) The transgenic mammal of claim 11 wherein the inhibition of the poly(ADP ribose) polymerase has been effected by a transgenic operation.

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16. (Amended) A method of identifying carcinogenic agents, comprising (i) administering one or more potential carcinogenic agents to a transgenic mammal having a genome comprising a DNA repair disturbance caused by inhibiting the poly(ADP ribose) polymerase, wherein said mammal is selected from the group consisting of transgenic mammals having a genome wherein the expression of poly (ADP ribose) polymerase is altered by an inserted gene encoding a dominant negative poly(ADP ribose) polymerase, and (ii) comparing said transgenic mammal administered one or more potential carcinogenic agents, with a transgenic mammal not administered said one or more potential carcinogenic agents, wherein development of tumor in the transgenic mammal administered said one or more potential carcinogenic agents, indicates that a potential carcinogenic agent is a carcinogenic agent.

Please add new claims 17-20, as follows:

17. A transgenic mouse, wherein a DNA construct comprising the human cytokeratin-14 promotor operably linked to the coding sequence of the DNA binding domain of human poly(ADP ribose) polymerase (EC.2.4.2.30) and polyadenylation signal of the human cytokeratin-14 gene is integrated into the genome of the transgenic mouse and wherein said DNA construct is the DNA construct of Figure 1 and wherein said DNA construct expresses a dominant negative poly(ADP ribose) polymerase in the cells of the basal layer of the skin of the transgenic mouse and wherein in said cells of the basal layer of the skin, the poly(ADP ribose) polymerase is inhibited by the dominant negative poly(ADP ribose) polymerase expressed by the DNA construct.

18. A method of identifying carcinogenic agents, comprising topically administering one or more potential carcinogenic agents to a transgenic mouse as claimed in claim 17, wherein, when said topical administering of said one or more potential carcinogenic agents to said transgenic mouse, compared to a transgenic mouse not administered the one or more potential carcinogenic agents, results in the development of skin tumors, said one or more carcinogenic agents is considered to comprise a carcinogenic agent.

19. A method of identifying carcinogenic agents, comprising administering one or more potential carcinogenic agents to a transgenic mammal in which poly(ADP ribose) polymerase is inhibited by a transgenic expression of a dominant negative mutant of poly(ADP ribose) polymerase, wherein, when said administering of said one or more potential carcinogenic agents to said transgenic mammal, compared to a transgenic mammal not administered the one or more potential carcinogenic agents, results in the development of tumors, said one or more carcinogenic agents is considered to comprise a carcinogenic agent.

20. A transgenic mammal in which poly(ADP ribose) polymerase is inhibited by a transgenic expression of a dominant negative mutant of poly(ADP ribose) polymerase.